Remarks

Applicants acknowledge Examiner's allowance of claims 25-30. Claims 25-34 are pending in the application. Claims 31 through 34 have been amended and claims 35-37 have been added. Support for the amendments and the new claims may be found throughout the specification. No new matter has been added.

In particular, support for new claim 35 may be found, for example, at page 17, lines 1-19, support for new claim 36 may be found, for example, at page 20, lines 26-32, and support for new claim 37 may be found, for example, at page 20, lines 9-23. Support for the amendments to claims 31 and 33 may be found, for example, at page 23, lines 20-28. Additional support for the new claims and claim amendments may be found in SEQ ID NOs: 1 and 2.

Amendment of claims should in no way be construed as an acquiescence to any of the Examiner's rejections. The amendments to the claims are being made solely to expedite prosecution of the present application and do not, and are not intended to, narrow the claims in anyway. Applicants reserve the option to further prosecute the same or similar claims in the instant or in a subsequent patent application.

Rejection of claims 31-34 under 35 U.S.C 112, first paragraph

The Examiner states that claims 31-34 stand rejected under 35 U.S.C. 112, first paragraph because, according to the Examiner, they describe subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the invention at the time the application was filed. The rejection is respectfully traversed.

The Examiner states that claims 31-34 "recite a polypeptide comprising a fragment of SEQ ID NO:2 comprising at least 30/50 amino acids." However, according to the Examiner, "the specification and claims do not indicate what distinguishing attributes are shared by the members of the genus." The Examiner further states that Applicants "have not described the function which is shared by the 30 consecutive amino acids of SEQ ID NO: 2 which would adequately describe the genus."

Applicants respectfully submit that the specification is replete with teachings of the structure of the Fab I protein, exemplary fragments thereof, and the functional characteristics of Fab I and Fab I fragments. More specifically, Fab I protein fragments are discussed on page 21, line 6 through page 24, line 2. For example, page 21, lines 24-26 describe a variety of 20 amino acid regions of the Fab I protein, either as individual fragments or as contiguous combinations thereof. At page 21, lines 27-30 the specification describes a variety of fragments that are highly homologous to other proteins, which would indicate a highly conserved region with an important enzymatic or structural function. The specification further discloses truncation mutants, page 21, lines 31-33 through page 22, lines 1-5, and degradation products of the polypeptides of the invention in the host cell, page 22, lines 5-7.

The subject patent application further teaches fragments characterized by structural attributes of Fab I (see page 22, lines 8-33 through page 23, lines 1-28). In particular, the specification contemplates fragments that comprise certain structural features, such as alpha helix forming regions, beta sheet regions, coil regions, hydrophobic regions, alpha amphipathic regions, beta amphipathic regions and flexible regions. Importantly, the patent specification specifically identifies regions of Fab I that correspond to such secondary structures.

Furthermore, the specification at page 23, lines 20-28, discloses polypeptide fragments that correspond to functional regions of the protein. In particular, the patent specification discusses fragments that retain a biological activity of Fab I.

Based on the arguments above, Applicants maintain that the specification discloses more than "a mere statement that [the fragments] are part of the invention and a reference to a potential method of isolating [the fragment]." Accordingly, the specification describes a representative number of Fab I fragments to describe the genus with sufficient detail to demonstrate that the inventors had possession of the claimed invention at the time of filing. Thus, reconsideration and withdrawal of this rejection is respectfully requested.

Rejection of claims 31-34 under 35 U.S.C. 102(e)

Claims 31-34 have been rejected under 35 U.S.C. § 102 (e) as being anticipated by Bailey et al. (U.S. Patent No. 6,403,337). The Examiner states that Bailey et al. "discloses a polypeptide of SEQ ID NO: 6 from *Staphylococcu aureus*" and teaches of "acceptable carriers for compositions and fusions with heterologous proteins (columns 102-111)." Furthermore, the Examiner states that "SEQ ID NO: 6 comprises amino acid residues 1-256 that are 99.5% identical over amino acid residues 1-256 of SEQ ID NO: 1 as instantly claimed."

In part, the sequences of Bailey et al. (SEQ ID NO: 6) and the instant invention (SEQ ID NO: 2) differ by an amino acid at position 191, so that SEQ ID NO: 2 of the instant application contains a glycine (G191) and SEQ ID NO: 6 of Bailey et al. contains a serine (S191). Applicants respectfully submit that it is their belief that SEQ ID NO: 2 of the instant application represents the wild-type polypeptide sequence not the Bailey et al sequence. In support of that conclusion, Applicants submit a BLAST analysis of SEQ ID NO: 2 (Appendix A), which reveals that out of 100 sequences that produced significant alignments, all 100 contained a glycine at position 191 (or the equivalent amino acid position in a related sequence). Accordingly, Applicants submit that Bailey et al does not render SEQ ID NO: 2 of the present invention obvious, in part because the location of the sequence difference at position 191 in the amino acid sequence is located in a region of homology among Fab I variants. A sequence alignment of Fab I proteins from various pathogens is provided in Appendix B.

Applicants further submit that the instant specification identifies regions of homology that represent domains of functional significance (see page 23, lines 20-26). The region flanking position 191 in Fab I is identified as highly conserved across species suggesting that it is important in protein function (Appendix B). In the reported *E. coli* Fab I protein, position 190 corresponds to position 191 of SEQ ID NO:2 of the present invention. Notably, this position is occupied by a glycine in both instances. The crystal structure of the *E. coli* Fab I protein has been solved (Qiu X, et al., (1999) Protein Science 8 (11): 2529-32). Applicants respectfully submit that according to the crystal structure, the relevant portion of which is provided in Appendix C, the glycine at position 190 (equivalent to position 191 of SEQ ID NO:2) forms part of a conserved triclosan binding site of Fab I. Triclosan is widely used as an antibacterial and

antifungal agent that is a component of toothpaste, soaps, cosmetics and textiles (Bhargava, et al., (1996) Am. J. Infect Control, 24:209-218). Given the conserved nature of this region, Applicants submit that non-conservative substitutions at this position are likely to affect the dimensions of the binding pocket and, concomitantly, the mechanics of substrate binding. As an example, it has been reported that a non-conservative mutation of a nearby phenylalanine to a cysteine, F204C, renders the *S. aureus* resistant to triclosan (Fan, F., et al., (2002) Antimicrob Agents Chemother, **46**(11): p. 3343-7). In addition, G191 has the further distinction of bordering on the co-factor binding site of the *E. coli* Fab I protein. Thus, amino acid substitutions at this position may affect the binding properties of the Fab I co-factor.

Based on the arguments above, Applicants maintain that Bailey et al. does not anticipate claims 31-34. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Conclusion

In view of the above remarks and the amendments to the claims, it is believed that this application is in condition for allowance. If a telephone conversation with Applicant's Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 832-1000.

Respectfully submitted,

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Dated: April 3, 2003

Copy of amended claims with changes marked thereon

Please amend claims 31 and 33 as set forth below:

31. **(Thrice Amended)** An isolated polypeptide fragment comprising at least 50 consecutive amino acids of SEQ ID NO: 2 wherein said polypeptide fragment comprises the amino acid at position 191 of SEQ ID NO: 2, wherein said amino acid is glycine or a conservative substitution thereof, and wherein the polypeptide fragment comprises at least one biological activity of Fab I.

33. **(Thrice Amended)** An isolated polypeptide fragment comprising at least 30 consecutive amino acids of SEQ ID NO: 2 wherein said polypeptide fragment comprises the amino acid at position 191 of SEQ ID NO: 2, wherein said amino acid is glycine or a conservative substitution thereof, and wherein the polypeptide fragment comprises at least one biological activity of Fab I.